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Recording of Corticospinal Evoked Potential for Optimum Placement of Motor Cortex Stimulation Electrodes in the Treatment of Post-stroke Pain

—Two Case Reports—

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Abstract

The corticospinal motor evoked potential (MEP) evoked by motor cortex stimulation was investigated as an intraoperative index for the placement of stimulation electrodes in the epidural space over the motor cortex for the treatment of post-stroke pain. A grid of plate electrodes was placed in the epidural space to cover the motor cortex, sensory cortex, and premotor cortex employing a magnetic resonance imaging-guided neuronavigation system in two patients with severe post-stroke pain in the right extremities, a 66-year-old man with dysesthesia manifesting as burning and aching sensation, and a 67-year-old woman with dysesthesia manifesting as pricking sensation. The D-wave of the corticospinal MEP was recorded with a flexible wire electrode placed in the epidural space of the spinal cord during anodal monopolar stimulation of each plate electrode under general anesthesia. The grid electrode was fixed in position with dural sutures and the craniotomy closed. The effect of pain reduction induced by anodal monopolar stimulation of the same plate electrodes was examined using the visual analogue scale (VAS) on a separate day in the awake state without anesthesia. Comparison of the percentage VAS reduction and the recorded amplitude of the D-wave employing the same stimulation electrode revealed significant correlations in Case 1 ($r = 0.828$, $p < 0.01$) and Case 2 ($r = 0.807$, $p < 0.01$). The grid electrode was then replaced with two RESUME electrodes over the hand and foot areas, and the optimum positions were identified by D-wave recording before electrode fixation. Both patients reported satisfactory pain alleviation with lower stimulation voltages than usually required for patients with similar symptoms. These results indicate the potential of D-wave recording as an intraoperative indicator for the placement of stimulating electrodes over the motor cortex for pain relief.

Key words: motor evoked potential, post-stroke pain, motor cortex stimulation, corticospinal motor evoked potential, D-wave

Introduction

Motor cortex stimulation therapy was first proposed for the treatment of post-stroke pain,[19-21] and subsequently numerous studies have examined the effectiveness for neuropathic pain and central pain.[2-4,7,8,11-13,16,17,22] In the large series, the long-term success rate for pain alleviation was about 50%. The pain control provided by motor cortex depends on stimulation of neuronal circuits mediated by corticospinal tract neurons originating from the motor cortex.[9] Activation of the thalamic nuclei directly connected with the motor and premotor cortices causes a cascade of synaptic events in pain-related structures receiving afferents from these nuclei, including the medial thalamus, anterior cingulate, and upper brainstem, and motor cortex stimulation attenuates the nociceptive spinal reflexes.[5] Motor cortex stimulation also produces significant transient inhibition of the responses of the spinal cord dorsal horn neu-

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rons to higher intensity mechanical stimuli without affecting the response to innocuous stimuli.[18] Therefore, at least part of the antinociceptive effect induced by motor cortex stimulation involves the corticospinal tract neurons originating from the motor cortex.

Correct placement of the cortical electrode, which induces the muscle twitches or muscle contractions, is most important to achieve effective pain relief in post-stroke pain.[9,21] The recommended position of the cortical stimulation electrode is over the painful area.[14,17,21] Various surgical techniques are available for the accurate placement of epidural or subdural electrodes over the motor cortex.[14,17,21] However, a standard method has not yet been established. Anatomical identification of the central sulcus by phase reversal of N20 with monitoring of the somatosensory evoked potential or magnetic resonance (MR) imaging-guided neuronavigation may allow exact positioning of the stimulation electrode on the precentral gyrus directly or epidurally. However, the activation of the corticospinal tract neurons originating from the motor cortex cannot be predicted. Moreover, anodal monopolar cortical stimulation activates vertically oriented pyramidal neurons,[1] whereas only cathodal bipolar cortical stimulation, which tends to excite the superficial horizontal fibers and cortical interneurons, is available from the implantable pulse generator approved for clinical use.

The corticospinal motor evoked potential (MEP) evoked by direct stimulation of the motor cortex can be recorded from the epidural space of the spinal cord, and has been used for the intraoperative monitoring of motor function.[9,23] The corticospinal MEP response consists of an initial D-wave and a later sequence of volleys termed I-waves.[1,15] The D-wave reflects impulses arising from direct activation of the axons of corticospinal tract neurons, whereas the I-waves reflect neurons via synaptic activity.

The present study examined the relationship between pain reduction on the visual analogue scale (VAS) and the recorded amplitude of the D-wave during stimulation of various points of the motor cortex to evaluate the D-wave as an index for the placement of the epidural electrode in the treatment of post-stroke pain.

Patients and Methods

This study included two patients, a 66-year-old man with post-stroke pain in the right extremities caused by left pons bleeding manifesting as dysesthesia with burning and aching sensation for 25 months (Case 1), and a 67-year-old woman with post-stroke pain in the right extremities caused by thalamic bleeding manifesting as dysesthesia with pricking sensation for 24 months (Case 2). Both patients felt most severe pain in the upper extremity. Both patients could walk unaided, and had grade 4 motor function of the right extremity by the muscle maneuver test (MMT).[23] Both patients gave informed consent for intraoperative monitoring of the corticospinal MEP and test stimulation employing a grid electrode implanted in the epidural space just over the motor cortex. The present study was approved by the Committee for Clinical Trials and Research in Humans of our university and by the Japanese Ministry of Health and Welfare as part of an advanced medical care program.

A flexible four-channel, platinum wire electrode (3487A PISCES-Quad; Medtronic, Inc., Minneapolis, Minn., U.S.A.) was inserted into the epidural space of the cervical vertebrae, at the C2 to C4 levels, on the day before the operation. The patient was placed in the abdominal prone position, and an 18-gauge Touhy needle included in the electrode package was inserted into the midline epidural space at the cervical and thoracic junction under radiographic control. The spinal epidural space was confirmed from the change of resistance observed during saline injection through the Touhy needle. The electrode was inserted into the epidural space with a stylet via the Touhy needle and advanced to the appropriate position under radiographic control. The stylet and Touhy needle were then removed, and the electrode was fixed with adhesive tape and a drape placed on the skin (Fig. 1).

On the next day, a craniotomy sufficient to expose the postcentral gyrus, precentral gyrus, and posterior parts of the superior, middle, and inferior frontal gyri was performed under general anesthesia with muscle relaxant and completely controlled ventilation. The grid electrode, comprising 20 plate electrodes of 5 mm diameter and each separated by 5 mm, with each of the plate electrodes embedded in thin and soft silicone material (Unique Medical Co., Ltd., Komae, Tokyo), was placed in the epidural space over the motor, sensory, and premotor cortices employing an MR imaging-guided neuronavigator (Fig. 2). The ground electrode was placed on the forehead. The cerebral cortex was stimulated utilizing each contact point of the grid electrode. The stimulation was applied as a monophasic square wave pulse of 0.2 msec duration delivered at 2 Hz, and anodal monopolar stimulation with an intensity of 30 mA was selected for monitoring of the D-wave. A recording electrode with four contact points was used for bipolar recording between adjacent contact

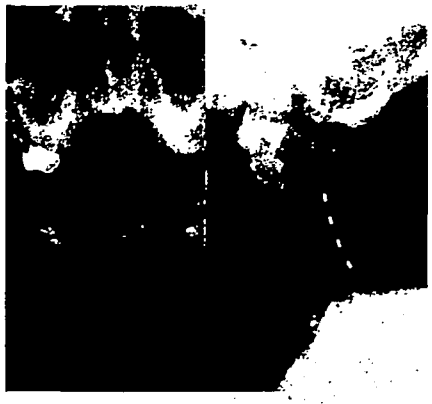

Fig. 1 Radiographs showing a four-channel wire electrode placed within the epidural space of the cervical spinal cord at the C2 to C4 levels.

Fig. 2 Radiograph showing an epidural grid electrode implanted in the epidural space for direct cortical stimulation, and the electrode in the epidural space of the cervical spinal cord (arrow). Same orientation as Fig. 4.

points, and the signals were fed into an amplifier with a band pass range of 5 Hz to 5 kHz and averaged for 32 sweeps using Synax 2100 (NEC Co., Tokyo).

After recording the corticospinal MEP, the epidural grid electrode was fixed to the dura with sutures at several points to maintain the grid electrode location, and the wound was closed. The effect on pain induced by monopolar anodal cortical stimulation employing the contact points of the grid electrode was examined using the VAS on another day in the awake state without anesthesia. This test stimulation used a frequency of 25 Hz with a

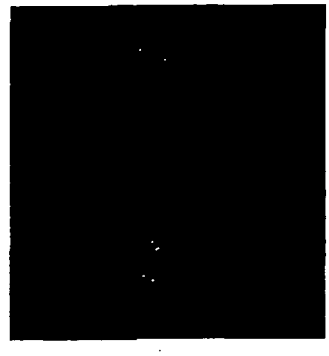

Fig. 3 Radiograph showing the two RESUME motor cortex stimulation electrodes placed on the hand and foot areas.

duration of 0.2 msec, and the best stimulation intensity was selected between 10 to 20 mA. The change of the VAS was expressed as percentage VAS reduction; calculated as (1 − VAS with stimulation/VAS without stimulation) × 100%. The percentage VAS reduction and the recorded amplitude of the D-wave using the same stimulating electrode were then compared by simple regression analysis.

After confirming that pain alleviation was obtained with cortical stimulation, chronic implantation of the electrode for motor cortex stimulation was performed under general anesthesia with muscle relaxant. Until this second operation, the recording electrode was left in the cervical epidural space. The epidural grid electrode was replaced with a four-channel plate electrode (3587A RESUME · II; Medtronic, Inc.), which has four contact points consisting of plate electrodes of 5 mm diameter and spaced 5 mm apart. The optimum location of the two RESUME electrodes for stimulation of the hand and foot areas was identified by monitoring the D-wave with bipolar stimulation of the most distant two contact points of the four (Fig. 3). After confirming the best location for the RESUME electrodes, which evoked the D-wave at the highest amplitude by bipolar stimulation, the edge of the RESUME electrode was sutured to the dura, to prevent movement of the electrode. This procedure was essential to ensure steady attachment between the dura and contact points. An implantable pulse generator was implanted under the anterior chest wall at the same time, and connected to the RESUME electrode with an extension cable.

Results

D-waves were detected after stimulation of 14 of the

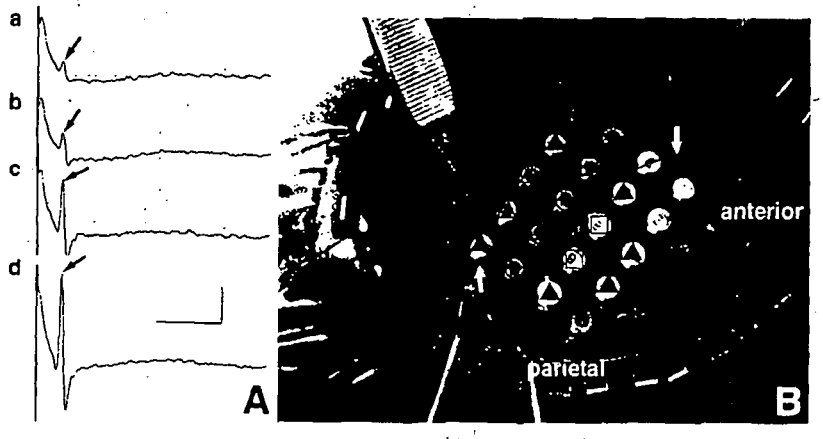

Fig. 4 **A: Representative D-waves (*arrows*) classified into amplitudes of under 2 μV (a), 2 to 5 μV (b), 5 to 10 μV (c), and over 10 μV (d). Time scale, 5 msec; amplitude, 5 μV. B: Photograph of the intraoperative epidural grid electrode placed over the sensory, primary motor, and premotor cortices in Case 1. The amplitude of the D-wave evoked by the stimulation of each plate electrode was classified as over 10 μV (*open circles*), 5 to 10 μV (*open squares*), 2 to 5 μV (*open triangles*), and under 2 μV (*closed triangles*). *Thick line*: Central sulcus estimated by magnetic resonance imaging-guided navigation.**

20 contact points of the grid electrode in Case 1, and 11 contact points in Case 2. The recorded amplitudes of the D-waves were classified into over 10 μV, 5 to 10 μV, 2 to 5 μV, and less than 2 μV (Fig. 4A). The evoked amplitudes of the D-waves were plotted on an intraoperative view of the grid electrode (Fig. 4B). The contact points which evoked D-wave amplitudes of over 10 μV were located just anterior to the central sulcus as estimated by MR imaging-guided neuronavigation.

Figure 5 illustrates the relationships between the recorded amplitude of the D-wave and the percentage VAS reduction in Cases 1 and 2. Simple regression analysis showed significant correlations in Case 1 ($r = 0.828$, $p < 0.01$) and Case 2 ($r = 0.807$, $p < 0.01$).

Discussion

The present study used high intensity anodal monopolar stimulation so that both the electrode contact areas and the surrounding cortical areas were stimulated together, thus stimulating a wider area of the cerebral cortex than previously,[23] so we could compare the amplitude of the D-wave with the percentage VAS reduction. The percentage VAS reduction was significantly correlated with the D-wave amplitude, indicating that D-wave recording provides an intraoperative guide for placing the stimulating electrode at the optimum position on the motor cortex.

Chronic implantation of the RESUME electrodes was performed in the epidural space exposed by the craniotomy. The electrodes were placed parallel to the sagittal sinus over the central sulcus in the foot area, and parallel to the central sulcus over the motor strip in the hand area. The optimum positions were identified by searching for the D-wave with the highest amplitude evoked by bipolar stimulation. Both patients complained of most severe pain in the upper extremity, but also of dysesthesia of the lower extremity. Therefore, both hand and foot areas were stimulated together, since it is important to induce muscle contraction or muscle twitch in the painful area for the motor cortex stimulation therapy.[10,19-22]

Our previous experience with patients with MMT of 4 suggested that the threshold intensity to induce muscle contraction under stimulation conditions of 25 Hz with 0.2 msec duration is 5.8 ± 0.9 V ($n = 10$). In the present patients, muscle contraction was induced at 2.9 V in Case 1 and 3.3 V in Case 2. Both patients were satisfied by the results of chronic motor cortex stimulation. These findings confirm the importance of identifying the optimum point for motor cortex stimulation therapy in the treatment of post-stroke pain.

Corticospinal MEP monitoring requires insertion of the recording electrode into the cervical epidural space. The recording electrode can be easily and safely placed in the epidural space by the same technique as used for transcutaneous spinal cord stimulation for the treatment of pain, and we have already

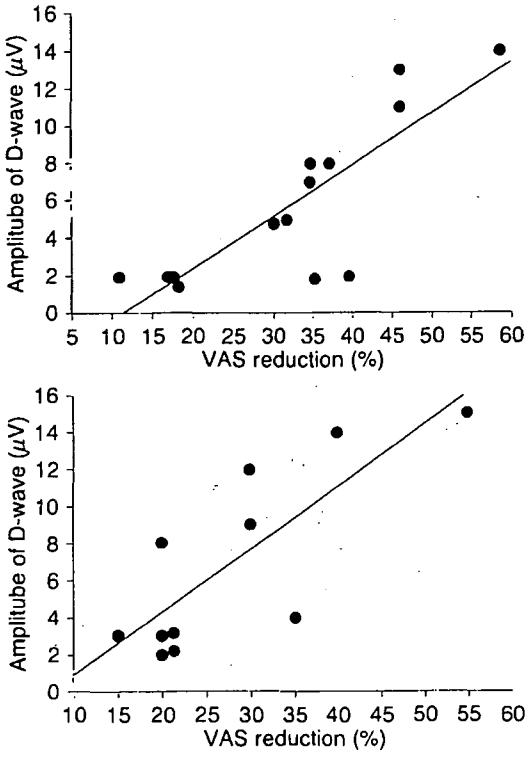

Fig. 5 Correlations of the recorded amplitude of the D-wave and the percentage visual analogue scale (VAS) reduction in Case 1 (upper) and Case 2 (lower). Simple regression analysis showed significant correlations in Case 1 ($Y = -3.033 + 0.274X$, $r = 0.828$, $p < 0.01$) and Case 2 ($Y = -2.575 + 0.339X$, $r = 0.807$, $p < 0.01$). Percentage VAS reduction = (1 − VAS with stimulation/VAS without stimulation) × 100%.

experienced over 250 cases without irreversible complications arising from such electrode insertion. Monitoring of the muscle responses to direct motor cortex stimulation is also useful for the monitoring of cerebral ischemia.[6] Another advantage is that, unlike muscle responses to motor cortex stimulation, the D-wave of the corticospinal MEP is resistant to surgical doses of anesthetics and is unaffected by muscle relaxants, apart from changes to the excitability of the spinal motor neurons, and so the amplitude can be easily correlated with the site of cortical stimulation.

The present study indicates that monitoring of the D-wave provides a good indicator of the optimum placement of the chronic electrode for the treatment of post-stroke pain, and thus allows implantation of the motor cortex stimulation electrode in a one-stage operation under general anesthesia.

Acknowledgment

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Thalamic deep brain stimulation for writer's cramp

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Object. Writer's cramp is a type of idiopathic focal hand dystonia characterized by muscle cramps that accompany execution of the writing task specifically. In this report, the authors describe the clinical outcome after thalamic deep brain stimulation (DBS) therapy in patients with writer's cramp and present an illustrative case with which they compare the effects of pallidal and thalamic stimulation. In addition to these results for the clinical effectiveness, they also examine the best point and pattern for therapeutic stimulation of the motor thalamus, including the nucleus ventrooralis (VO) and the ventralis intermedius nucleus (VIM), for writer's cramp.

Methods. The authors applied thalamic DBS in five patients with writer's cramp. The inclusion criteria for the DBS trial in this disorder were a diagnosis of idiopathic writer's cramp and the absence of a positive response to medication. The exclusion criteria included significant cognitive dysfunction, active psychiatric symptoms, and evidence of other central nervous system diseases or other medical disorders. In one of the cases, DBS leads were implanted into both the globus pallidus internus and the VO/VIM, and test stimulation was performed for 1 week. The authors thus had an opportunity to compare the effects of pallidal and thalamic stimulation in this patient.

Results. Immediately after the initiation of thalamic stimulation, the neurological deficits associated with writer's cramp were improved in all five cases. Postoperatively all preoperative scale scores indicating the seriousness of the writer's cramp were significantly lower ($p < 0.001$). In the patient in whom two DBS leads were implanted, the clinical effect of thalamic stimulation was better than that of pallidal stimulation. During the thalamic stimulation, the maximum effect was obtained when stimulation was applied to both the VO and the VIM widely, compared with being applied only within the VO.

Conclusions. The authors successfully treated patients with writer's cramp by thalamic DBS. Insofar as they are aware, this is the first series in which writer's cramp has been treated with DBS. Thalamic stimulation appears to be a safe and valuable therapeutic option for writer's cramp. *(DOI: 10.3171/JNS-07/11/0977)*

KEY WORDS • **deep brain stimulation** • **focal dystonia** • **thalamotomy** • **writer's cramp**

WRITER'S cramp is a representative type of idiopathic focal hand dystonia characterized by muscle cramps that accompany execution of the writing task specifically. There has been renewed interest in neurosurgical procedures for the treatment of dystonia over the past several years. In particular, DBS has received increasing attention as a therapeutic option for patients with dystonia.[4,22] This treatment modality offers several potential benefits over radiofrequency lesioning.[9] The functional location and size of the focus of stimulation can be changed and adjusted to various pathological states. Pallidal stimulation is one of the most promising new therapies for the treatment of dystonia. The VO in the thalamus, however, has been recognized as an appropriate target for radiofrequency ablation in patients with writer's cramp.[1,6,14,16,17] In this report, we describe the clinical outcome of thalamic stimulation in patients treated for writer's cramp, and we present an illustrative case that allows us to compare the effects of stimulation of the GPI and VO/VIM. In addition to these results for the clinical effectiveness, we also describe the results of an investigation regarding the best point and pattern of stimulation of the VO/VIM for writer's cramp.

Abbreviations used in this paper: AC = anterior commissure; BFMDR = Burke-Fahn-Marsden Dystonia Rating; DBS = deep brain stimulation; GPI = globus pallidus internus; MR = magnetic resonance; PC = posterior commissure; VC = ventralis caudalis nucleus; VIM = ventralis intermedius nucleus; VO = nucleus ventrooralis.

Clinical Material and Methods

Patient Population

We applied thalamic stimulation in five patients with writer's cramp. The inclusion criteria for the DBS trial were that the patient was diagnosed as having idiopathic writer's cramp and did not demonstrate evidence of a good response to medical treatment. The exclusion criteria included significant cognitive dysfunction, active psychiatric symptoms, and evidence of other central nervous system diseases or other medical disorders. The DBS lead was implanted unilaterally in all cases. In one case, two DBS leads were implanted: one each into the GPI and the VO/VIM in a single

operation. We thus had an opportunity to compare the effects of GPI and VO/VIM stimulation in this patient during a 1-week test stimulation period.

Surgical Techniques

A Leksell G head frame (Elekta Instruments) was used for the surgery. Magnetic resonance images (1-mm-thick slices) were obtained, and the AC and PC were identified on the Leksell SurgiPlan (Elekta), a customized software program for functional stereotaxy. The target was approached from a bur hole perforated anteriorly at an angle of 45 to 55° to the AC–PC line and 0 to 12.5° to the vertical plane. Three-dimensional trajectory visualization on a digitized version of the Schaltenbrand–Wahren atlas[15] was used to confirm the structures that the electrode passed.

The first trajectory was directed toward the anterior aspect of the PC, on the level of the AC–PC line, at 15 mm lateral to the midline, or 9 mm lateral to the wall of the third ventricle. Following this procedure, a semimicroelectrode recording was performed. Certain cells responding to passive joint movements of the contralateral limbs, caused by deep sensation, and cells responding to light touch on the skin of the face and contralateral limbs, caused by cutaneous sensation, appeared on this trajectory. Based on these neurophysiological findings, we defined the thalamic VIM–VC border as a vertical line on this trajectory. Cells responding to cutaneous sensation were usually observed posterior to the VIM–VC border, and semimicrostimulation produced paresthesia in such an area. The VIM–VC border determined by these observations was located 1.9 to 5.5 mm anterior to the anterior aspect of the PC. The second trajectory was directed toward the VIM–VC border, on the level of the AC–PC line, at 12 to 15 mm lateral to the midline, confirming that the trajectory was located medially to the VO/VIM–internal capsule border, as estimated by MR imaging. The locations of each thalamic nucleus were also determined using a digitalized human brain atlas adjusted to the MR image of each patient's brain.

A DBS electrode (Medtronic, Inc.) with four contact points, numbered 0 to 3 sequentially from the most distal contact (0) to the most proximal contact (3), was placed through the frontal bur hole into the thalamic VO and VIM nuclei. Each contact of the electrode was 1.5 mm long, and the contacts were 1.5 mm apart from each other. We placed Contact 0 at the VIM–VC border on the level of the AC–PC line, and 12 to 15 mm lateral to the midline, in most cases. This usually resulted in Contact 1 being located within the ventral VIM, Contact 2 within the central VIM or the posterior VO, and Contact 3 within the dorsal part of the posterior VO or the anterior VO (Fig. 1).

After implantation of the electrode, postoperative MR imaging was performed, and the stereotactic coordinates of the center of each contact were determined. The locations of the DBS electrodes and the VIM–VC border, as identified from neurophysiological data, were then reconstructed on the stereotactic coordinates of the postoperative MR imaging studies.

Stimulation Procedures

During the test stimulation period of approximately 1 week, electrical stimulation was delivered as monophasic pulses with a duration ranging from 0.05 to 0.21 msec. The frequency and intensity of stimulation were usually within the range of 90 to 185 Hz and 1.0 to 3.0 V, respectively. The DBS system, including an Implantable Pulse Generator (Medtronic), was internalized when satisfactory control of the writer's cramp was achieved during the test stimulation period. After internalization of the DBS system, we attempted to detect the most effective contact for monopolar stimulation. Subsequently, we performed bipolar stimulation with various combinations of contacts including the most effective contact of monopolar stimulation. The selection of contacts and parameters for the DBS was modified by the physicians at each follow-up visit, based on the neurological findings and the patient's own reports on improvement of the writer's cramp symptoms.

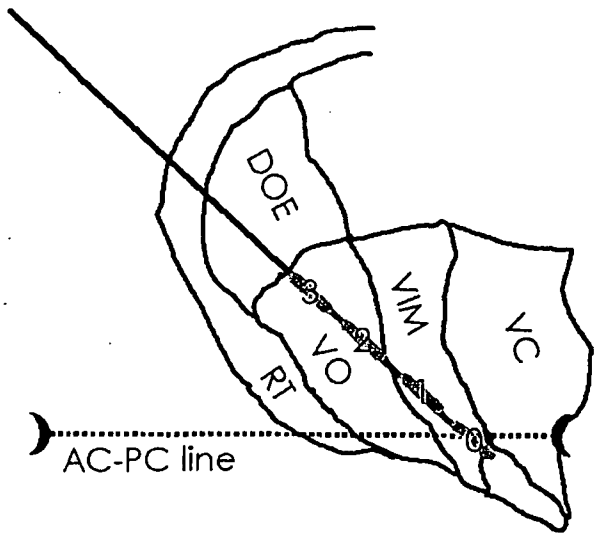

FIG. 1. Schema showing the Medtronic DBS electrode with four contact points, numbered 0 to 3 sequentially from the most distal (0) to the most proximal (3). We placed Contact 0 at the VIM–VC border on the level of the AC–PC line in most cases. This usually resulted in Contact 1 being located within the ventral VIM, Contact 2 within the central VIM or posterior VO, and Contact 3 within the dorsal part of the posterior VO or anterior VO. DOE = nucleus dorsooralis externus; RT = nucleus reticularis thalami.

Clinical Evaluation Procedures

The handwriting domain of the disability domain of the BFMDR Scale was used to evaluate patients' pre- and postoperative neurological conditions.[3] This handwriting scale is set such that normal writing receives a score of 0; slight difficulty, 1; almost illegible writing, 2; illegible writing, 3; and unable to grasp to maintain a hold on a pen, 4. Evaluations were performed using this scale preoperatively, as well as at 1 and 4 weeks and at 3, 12, and 24 months after the surgery.

We also took into consideration the patient's own subjective reports on the smoothness of writing when evaluating effects. Based on these reports, we defined the most effective combination of contacts and stimulation parameters for DBS. Also, the overall state of the letters that a patient wrote and the speed of writing were considered in the evaluation to define the appropriate mode of stimulation.

Mean results are presented ± the standard deviations.

Results

We analyzed data obtained after DBS electrode implantation in five patients with writer's cramp. The clinical characteristics and BMFDR handwriting scale scores are summarized in Table 1. The median age of the patients at surgery was 46.6 years (range 26–73 years). The median age at the onset of focal hand dystonic symptoms was 34.8 years (range 21–48 years), and the median duration of the disease was 11.8 years (range 2–25 years). In all cases the disorder was refractory to any medication. Two of the patients received botulinum toxin injection; they experienced improvement immediately after botulinum toxin injection, but the effect was short lived and did not satisfy their requirements.

As already mentioned, in the first patient we implanted two DBS leads: one each into the GPI and the VO/VIM. Based on a comparison of the results in this case, we considered thalamic stimulation to be superior to pallidal stimulation, and we adopted thalamic stimulation for use in the subsequent cases. The mean (± standard deviation) coordinates of the most distal contact of the electrodes (Contact 0) were established as 13.5 ± 1.5 mm lateral to the midline, 5.0 ± 1.1 mm anterior to the PC, and 0.9 ± 0.5 mm below the AC–PC line. We usually used one or two distal contacts as the cathode with monopolar polarity, or one distal contact as the cathode and a proximal contact as the anode with bipolar stimulation. In such situations, the stimulation parameters, including the intensity, frequency, and pulse width, were adjusted.

At 4 weeks, all five electrodes were set at 135 Hz. At 12 months, three were set at 135 Hz, one at 150 Hz, and one at 185 Hz. The mean voltage was 2.8 ± 1.3 V at 4 weeks and 2.7 ± 1.0 V at 12 months. The mean pulse width decreased from 210.0 ± 49.0 μsec at 4 weeks to 165.0 ± 57.4 μsec at 12 months. After undertaking the trial of some stimulation measures, we used bipolar stimulation in all of these patients at 12 months because of its better results. The mean preoperative handwriting score of the BFMDR instrument was 3.2 ± 0.45 in these patients. Immediately after the initiation of DBS, the score improved, to 0.4 ± 0.55, which was significantly lower than the preoperative value ($p < 0.001$, Wilcoxon t-test). The improvement in the score was maintained in subsequent evaluations at 24 months (Table 1).

We also investigated the best points for effective stimulation. We evaluated combinations of active contacts as appropriate clinical conditions for writing. The efficacy and combinations of contacts used for stimulation are summarized in Table 2. Based on our observations and each patient's subjective feelings, the bipolar stimulation of areas including VO and VIM with Cathode 0 and Anode 3 represented the most suitable combination for achieving substantial effectiveness. The mean improvement rate determined using the handwriting scale under these stimulation conditions was 91.0 ± 9.9%. The bipolar stimulation of VIM with Cathode 0 and Anode 1, however, showed an average improvement rate of 76.6 ± 22.4%, and the stimulation of VO with Cathode 2 and Anode 3 exhibited a mean improvement rate of 70.0 ± 18.3%. In the case of monopolar stimulation, the improvement rate of Stimulations 0 and 1 was 88.4 ± 16.1%; that of Stimulation 2 was 70.2 ± 18.2%; and that of Stimulation 3 was 13.2 ± 18.1%.

TABLE 1

*Clinical characteristics and BMFDR Scale scores obtained in the patients with writer's cramp**

Case No.	Age (yrs), Sex	Duration of Symptoms (yrs)	BMFDR Scale Score		
			Preop	4 Wks	24 Mos
1	40, M	10	3	0	0
2	42, M	2	3	0	0
3	73, M	25	4	1	1
4	26, M	5	3	0	0
5	52, M	17	3	0	0

* The BMFDR handwriting scale: 0 (best) to 4 (worst).

Stimulation with the contacts on the distal side tended to be relatively effective compared with that involving the proximal contacts in the case of monopolar stimulation. This suggests that stimulation applied to the VIM was more effective than that applied to the VO. However, the most effective mode of monopolar stimulation was relatively less effective than the most effective combination of contacts of the bipolar stimulation. Based on these results, bipolar stimulation employing the cathode on the anterior side of the VIM, with broad stimulation of the thalamic VO and VIM, appears to represent the best stimulation pattern for writer's cramp.

Illustrative Case

History. This 40-year-old man was referred to our hospital in 2001. He presented with severe stiffness in the right hand that appeared only during the handwriting task. The severity of his writing disability had gradually progressed over a period of 2 years. He had consulted a neurologist, who had diagnosed dystonic writer's cramp. This pathological condition was completely refractory to medical treatment.

Examination. Neurological examination demonstrated a severe abnormal muscle contraction in the right hand that was induced during handwriting. The stiffness and involuntary muscle contractions were present when the patient adopted the writing posture, and these deficits increased in intensity as he continued to hold a pen and write. His

TABLE 2

*Combinations of contacts used for DBS**

Contact Combination	Case No.				
	1	2	3	4	5
bipolar					
0(−), 3(+)	ME	ME	ME	ME	ME
1(−), 3(+)	SME	SME			
0(−), 1(+)					
1(−), 0(+)					
monopolar					
0(−), case(+)				SME	
1(−), case(+)			SME		SME
2(−), case(+)					
3(−), case(+)					

* ME = most effective; SME = second ME.

BFMDR Scale handwriting score was 4 preoperatively. His physical and mental conditions were completely normal. A brain MR imaging study revealed no abnormal findings, and other laboratory investigations demonstrated normal results. His personal and family histories were unremarkable.

Surgery. Two quadripolar electrodes for DBS were implanted: one into the left VO/VIM and the other into the GPI, after injection of a local anesthetic (Fig. 2). The coordinates of the tentative target points in the VO/VIM and the GPI were defined on a digitized version of a human brain atlas. Also, microrecordings were performed to monitor the extracellular activities in the vicinity of both tentative target points. The target for the VO/VIM was localized 6.5 mm anterior to the PC, 0.5 mm inferior to the AC–PC line, and 13.5 mm distant from the midline of the brain. The target for the GPI was localized at a point in the midcommissural point, 5 mm inferior to the AC–PC line, and 18 mm distant from the midline of the brain. We performed intraoperative neurological evaluations at the different DBS lead sites while the patient was writing. An immediate effect was clearly noted during VO/VIM stimulation, which appeared to be better than GPI stimulation. The gradual effects of GPI DBS, however, were observed, and this could not be denied because of the intraoperative neurological findings. We decided therefore to implant a DBS lead into each of the VO/VIM and the GPI in this, the first case. After the surgery, we performed a stimulation test for 1 week and carefully compared the effectiveness of VO/VIM and GPI stimulation.

Postoperative Examination and Course. Over the next week, various stimulation patterns were attempted to confirm the clinical effects and to compare the effects obtained with the two targets. Figure 3 shows the letters written presurgically, during VO/VIM stimulation, and during GPI stimulation. Based on the improvement rate on the handwriting scale, the patient's subjective feelings, and the entirety of letters written by the patient, we decided to connect the VO/VIM–DBS lead with an implantable pulse generator after the 1-week test stimulation. Considering the decrease in the thalamic stimulation effect, a lead for pallidal stimulation was implanted in the subgaleal space around the bur hole without connection to the pulse generator. The patient exhibited no surgery-related complications or stimulation-induced adverse effects due to the effective stimulation parameters.

FIG. 2. Radiograph demonstrating the two DBS leads implanted at the VO/VIM and GPI in the same patient.

Discussion

Writer's cramp has been regarded as a type of primary focal hand dystonia. Clinically, it involves severe difficulty in the continuation of writing, which is produced by spasm of the fingers that hold the writing instrument or by spasm of the entire hand. In general, the symptoms of writer's cramp are refractory to medical treatment. Attempting to achieve temporary improvement, intramuscular injections of botulinus toxin have been performed, but symptom recurrence is the rule, and the response to repetitive injection is sometimes reduced effectiveness. The authors of several reports have suggested the usefulness of stereotactic thalamotomy against dystonic hand cramping. Stereotactic thalamotomy was first introduced as a treatment for writer's cramp by Siegfreid et al.[17] Its successful therapeutic effect in patients with writer's cramp was thereafter reported in two studies.[1,14] Recently, Goto et al.[6] indicated that writer's cramp could be markedly relieved after stereotactic thalamotomy of the anterior VO and the posterior VO of the thalamus. Also, Taira and Hori[18] obtained satisfactory results in 12 patients with writer's cramp using this procedure, and emphasized the validity of stereotactic VO thalamotomy for writer's cramp. More recently, Shibata et al.[16] have described a case of medication-refractory writer's cramp in which the patient was successfully treated by stereotactic VO thalamotomy. However, there has been concern that such a destructive procedure might cause irreversible adverse effects. Chronic DBS therapy, in contrast, is currently considered an effective alternative to thalamotomy and/or pallidotomy, offering the advantages of reversibility, adaptability to changing clinical situations, and being probably associated with a lower incidence of postsurgical neurological deficits.[2,19]

There is cause to assert the superiority of thalamic DBS over thalamotomy as a treatment for writer's cramp. The stereotactic targeting strategies differ between thalamic DBS and thalamotomy.[9] In thalamotomy, a minimal radiofrequency lesion is created within the most appropriate site, providing maximal benefits without any side effects. This strategy depends on the assumption that there is a concentrated cluster of neural elements that are responsible for the pathological condition. However, this assumption is not necessarily true—such neural elements may sometimes spread out across wide areas. Thalamic DBS is not based on such an assumption. The thalamic electrode can be arranged in such a way that a wide area can be stimulated, if necessary.

In the present study the results obtained for the selection of active contacts suggest that bipolar stimulation, which covered a wide area of the VO/VIM, appeared to be the most appropriate pattern of therapeutic stimulation. In contrast, radiofrequency-induced lesions for thalamotomy cannot be arranged in such a way that a wide area is covered because of the inevitable occurrence of adverse effects. For

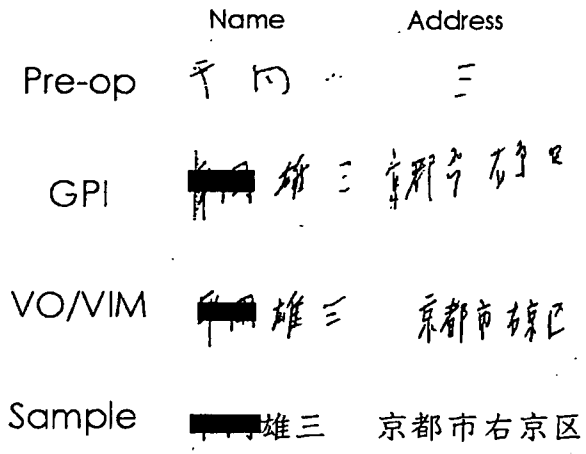

FIG. 3. Letters written by the patient presurgically, during VO/VIM stimulation, and during GPI stimulation, along with sample printed Japanese letters for comparison.

these reasons, we consider thalamic DBS to offer a more suitable therapy for writer's cramp than thalamotomy.

In addition, the concept of DBS of the GPI has frequently been introduced as a treatment for dystonic movement disorders over the past several years.[5,8,20,21] A prospective controlled multicenter study of this treatment modality in patients with primary generalized dystonia has already been published, and its usefulness for such treatment has been confirmed.[22] The authors of other papers have described the usefulness of GPI DBS as a treatment for dystonia—not only generalized dystonia but also other types, including focal or segmental dystonia.[10-13] Based on these data, GPI DBS appears to be an attractive treatment for writer's cramp, which is considered to be a form of focal hand dystonia. Choosing, as a target, between the GPI or the VO/VIM was thus not easy in our first case, and we therefore implanted two electrodes, one into the VO/VIM and one into the GPI.

Comparison of the results obtained with each of these two electrodes showed that thalamic stimulation was more effective than GPI DBS in treating writer's cramp. Since the successful outcome we observed after thalamic stimulation in our initial case, we have used this procedure to treat writer's cramp in four other patients, and the outcomes in all five cases were most gratifying. There was no surgery-related death or morbidity, and no stimulation-induced adverse effects. In view of these results, thalamic stimulation is thought to represent a useful treatment for writer's cramp.

Despite the various attempts at treatment, the pathophysiology of writer's cramp remains unclear. Several speculations concerning its background mechanisms have been made. Kaji et al.[7] suggested that a disorder of a motor subroutine might exist in the motor cortex–basal ganglia–thalamus-cortex loop in patients with dystonia. Moreover, a disorder of sensorimotor functional integration during motor tasks induces dystonic involuntary movements.[7,23] Writer's cramp could involve a functional abnormality of such a motor loop, as well as other dystonias during the writing task specifically. Improvement following stimulation of the motor thalamus is considered to be a result of normalization of abnormal activities in the pallidothalamocortical motor circuit. According to the description offered by Taira and Hori,[18] it is reasonable to infer that VO stimulation interrupts a functional abnormality of the cortex motor loop in an individual's writer's cramp, because the VO receives significant input from the GPI. However, we observed that stimulation that included the VIM, which receives input mainly from the cerebellum, more effectively improved writer's cramp. We cannot provide any evidence to explain this outcome, but the result itself indicates that both the basal ganglia–thalamus loop and the cerebellum are associated with writer's cramp. Greater experience with this treatment is needed to confirm this result. Also, additional studies are needed to determine the detailed pathophysiology of writer's cramp and the mechanisms of the DBS effects on such a pathological condition.

Conclusions

We have described five cases of writer's cramp in patients in whom thalamic DBS successfully resolved symptoms. Insofar as we are aware, this is the first series in which writer's cramp was treated using DBS therapy. In one case that provided an opportunity for us to compare the respective effects of VO/VIM and GPI stimulation, VO/VIM stimulation yielded the better effect. Also, the maximum effect was obtained when the stimulation widely covered the area from the VO to the VIM. Thalamic stimulation appears to represent a valuable therapeutic option, and the success achieved with this surgical treatment leads us to view writer's cramp from a new perspective.

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講　座 (Seminar)

中枢性疼痛に対するケタミン点滴療法

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要　旨
ケタミンを用いたドラッグチャレンジテストの結果を基にして，中枢性疼痛に対するケタミン点滴療法を施行した．ドラッグチャレンジテストでketamine-sensitiveな中枢性疼痛症例では，開始6カ月後の患者満足度調査で81%の症例が治療の継続を希望した．また，長期投与でもケタミン耐性は認められず，血液・生化学検査でも異常を認めない．ケタミン点滴療法は，難治性の中枢性疼痛の治療法として有用である．　(ペインクリニック 28：560-565，2007)
キーワード：ケタミン，中枢性疼痛，ドラッグチャレンジテスト

はじめに

中枢性疼痛の意味するところは中枢神経の損傷後に出現する疼痛（中枢性の求心路遮断痛）であり，視床痛，Wallenberg症候群，脊髄損傷後疼痛などが代表例として挙げられる．

知覚求心路の切断後に中枢側ニューロンに過剰放電が出現することは，脊髄後根切断後に脊髄後角内でニューロンの過剰活動を記録したLoeserら[1]（1967年）の報告以来，脊髄後角，三叉神経核，視床，大脳皮質知覚領など多くの部位で確認されている[2,3]．中枢神経損傷後疼痛の出現には，i）このニューロンの過剰活動が重要な役割を担っていること，ii）このニューロンの過剰活動の発現に，興奮性アミノ酸が関与していること，iii）特に知覚求心路の遮断後に著明であること，などが報告されている[4]．臨床的にも，興奮性アミノ酸のNMDA受容体の遮断薬であるケタミンならびに興奮性アミノ酸のシナプス伝達を抑制するバルビタール薬の効果が確認されている[5-7]．

われわれは，中枢性疼痛の薬理学的背景を明らかにする目的でドラッグチャレンジテストを行ってきた[8,9]．このドラッグチャレンジテストによってketamine-sensitiveと判定された中枢性疼痛症例についてケタミンの点滴療法を行ったので，その方法と効果について報告する．

1．ケタミンを用いたドラッグチャレンジテストの目的と方法

中枢性疼痛症例の治療方針を決定するためには，ドラッグチャレンジテスト[8,9]が有用であ

〈Seminar〉
Ketamine drip infusion therapy for the treatment of central pain
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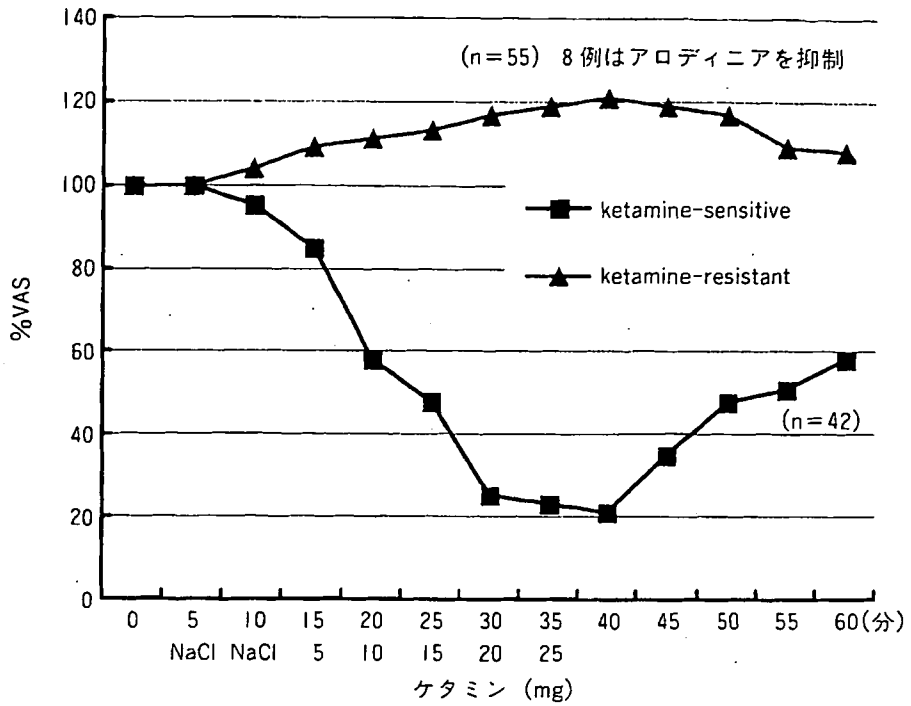

図1　102例の中枢性疼痛に対するケタミンテスト
%VAS＝ケタミン投与後VAS／ケタミン投与前VAS.
42例がketamine-sensitive, 55例がketamine-resistantであった. 自発痛の変化からketamine-resistantと判定された症例の中でも, 8例はアロデニアが著しく抑制されていた

る. われわれは, visual analogue scale (VAS) で痛みの評価を行い, 薬物投与によるVASの変化を比較している. この評価法の特徴は, プラセボ投与から始め, 少量ずつ段階的に薬物を投与するので, 少量から連続的に多量投与までの効果を確認できることである. 患者の訴える疼痛が, どのような薬物に, どの程度の投与量で, どの程度反応するか, または全く反応しないかを明らかにすることができる.

ケタミンテストは, 5分間隔で生理食塩水を2回投与後, 同様に5分間隔で塩酸ケタミン (ketamine hydrochloride) を5 mg, 合計25 mgまで静脈内投与する. モルヒネテストは, 同様に5分間隔で塩酸モルヒネ (morphine hydrochloride) 3 mgを合計18 mgまで静脈内投与し, チアミラールテストは, 同様に50 mgのチアミラールナトリウム (thiamylal sodium) (現在はチオペンタール：thiopental sodium) を, 5分間隔で合計250 mgまで静脈内投与している. 途中で入眠した場合は, その時点で中止する. また, 薬物投与前と比較して, VASが40%以上減少した症例をsensitive case, 40%以下の症例をresistant caseとしている.

2. ドラッグチャレンジテストの対象と結果

対象は中枢性疼痛102症例で, 男性62症例, 女性40症例であった. 年齢は25～79歳, 平均59歳であった. 原因疾患は, 脳血管障害後疼痛90症例 (梗塞症例24症例, 出血症例66症例), 頭部外傷後疼痛2症例, 脊髄損傷後疼痛10症例であった.

ケタミンテストの結果では, 42症例がketamine-sensitiveで, 55症例がketamine-resistantと判定された, 5症例は生理食塩水に反応するなどの判別困難例であった. 図1は, ketamine-sensitive症例とketamine-resis-

表1　ケタミン点滴療法（日本大学医学部脳神経外科）

1.生理食塩水 100 ml＋ケタラール®　20 mg（0.33 mg/kg）
　1時間かけて drip infusion，2週に1度（外来通院）

2.塩酸マプロチニン（ルジオミール®）30 mg/日
　ブロマゼパム（レキソタン®）6 mg/日
　カルバマゼピン（テグレトール®）300 mg/日
　内服（症状によって投与量の調整）

Morphine-sensitive で希望する症例には
3.経口モルヒネ（MS-コンチン®）30 mg/日

tant 症例における経時的な VAS の変化の平均値を表したものであるが，ketamine-sensitive な群では，ケタミン 20 mg の投与によって VAS が 70%以上減少し，それ以上の投与量を用いても明らかな変化を認めなかった．一方，ketamine-resistant 群では辺縁系に対する作用のためと考えられるが，逆に VAS が増加する症例が存在した．しかし，自発痛が増加したと訴えた症例の中でも身体各部位の評価を行うと，8例ではアロディニアが著しく抑制されていた．これらの結果を総合すると，ケタミンは約 50%の中枢性疼痛に有効であることが確認された．

3．ケタミン点滴療法の対象と方法

ドラッグチャレンジテストで ketamine-sensitive な症例に対して，100 ml の生理食塩水に 20 mg のケタミン(ケタラール®，0.33 mg/Kg)を加え，約1時間かけて点滴した．通常は2週間ごとに外来で点滴投与を行うこととし，患者の希望によって1～4週に1度の選択も可能とした．併用薬は塩酸マプロチニン（ルジオミール®）30 mg/日，ブロマゼパム（レキソタン®）6 mg/日，カルバマゼピン(テグレトール®)300 mg/日とし，morphine-sensitive で経口モルヒネを希望した症例にはモルヒネ(MS コンチン®)30 mg/日を投与した（表1）．

ケタミン点滴療法の対象は脳血管障害後疼痛 26 症例で，大脳皮質運動野刺激[9-11]を施行している症例6症例を含んでいる．原因は視床痛 24 症例（出血 18 例，梗塞 6 例）とワレンベルグ症候群2症例で，年齢は 46～75 歳で，平均 59.9 歳，男性 17 症例と女性 9 症例であった．

4．ケタミン点滴療法の効果

ケタミン点滴後に明らかに疼痛が抑制される持続時間は1～6時間以内が最も多く，24 時間以内が 77%であったが，24 時間以上持続するものも 23%存在した（図2）．

長期的な効果に対する検討では，ケタミン点滴開始6カ月後に行った患者満足度調査では，疼痛のコントロールに有用であることを自覚し，6カ月以上の継続を希望したもの 21 症例(81%)，疼痛のコントロールが一過性のため中止を希望したもの5症例（19%）であった．また，ケタミン点滴開始3年後に疼痛自体が消失した症例が1症例存在し，モルヒネの併用が有効であった症例は 10 症例中 6 症例であった．

長期投与によるケタミン耐性の有無についての検討では，20 mg で開始した 26 症例中，6カ月後も 20 mg が 19 症例，21～30 mg が5症例，10～19 mg が2症例で，モルヒネのような耐性は認めなかった（図3）．

問題点としては，ケタミンの点滴によって情動面の変化を呈する症例が存在したが，投与量ならびに投与時間の調整によってコントロールが可能であった．また，血液・生化学検査で異常が出現し，治療を中止した症例はいなかった．

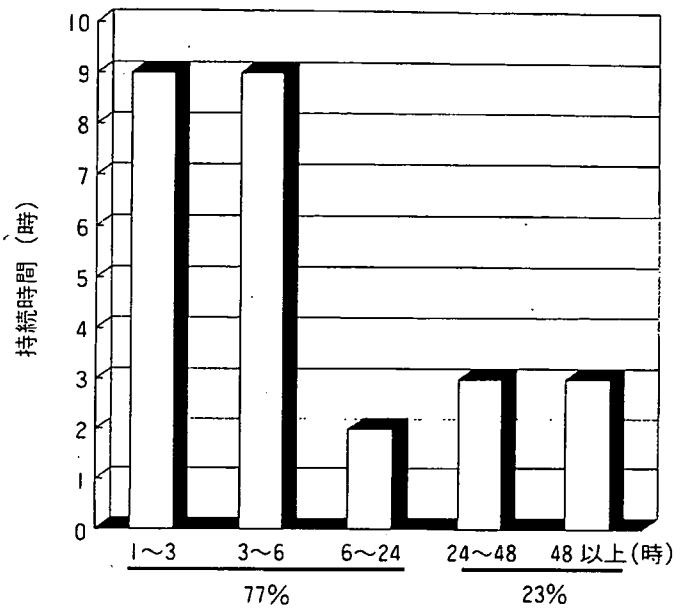

図2　ケタミン点滴療法における直接の持続時間
直接効果が24時間以内のものが77%で，24時間以上持続するものが23%であった

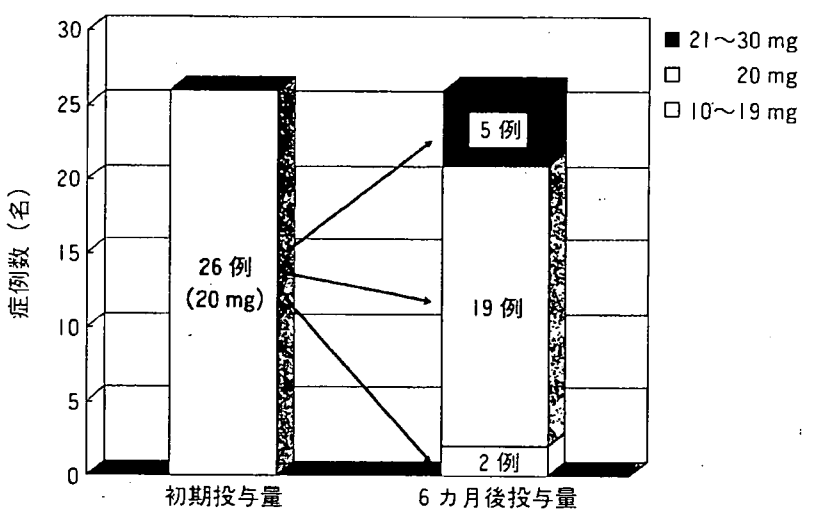

図3　ケタミン点滴療法におけるケタミン投与量の変化

5．ケタミン点滴療法の意義

ケタミン点滴療法では効果の持続時間に個人差があり，わずか数時間のものから数日間持続するものまで存在した．効果の持続時間が短い症例でも，一度疼痛を軽減することが疼痛の管理には重要であり，これによって精神的な安定を得られるという症例が多い．また，central sensitizationの解除にも有効であると考えられる[12-14]．ケタミンの持つ解離性麻酔薬としての性質から情動面の変化を呈する症例も存在したが，適切な投与量と投与時間を選択することによって，有効な治療効果を得ることができる．ケタミン点滴療法の併用薬として，抗うつ薬，抗不安薬，抗てんかん薬を用いたが，三環系抗うつ薬は，脳のシナプス間隙に放出された神経伝達物質のモノアミン（ノルアドレナリン：

NA，セロトニン：5-HTなど)のシナプス前神経終末への再取り込みを抑制し，シナプス間隙のモノアミンを増加させることによって，シナプス後受容体に対する作用を増強するとともに，長期投与によるシナプス後受容体の減少作用 (down regulation) も効果発現に関与しているものと考えられている．四環系抗うつ薬はシナプス前膜受容体，α_2受容体（自己受容体：オートレセプターとして自らNAの遊離を調整している)との結合を遮断して，NAの遊離を促進することが報告されている．疼痛に対する脳幹から脊髄後核への下行性の痛み抑制に5-HTやNAが重要な役割を担っていることが実験的に証明されているが，中枢性疼痛に対する下行性の痛み抑制系の関与については，現在も明確ではない[15]．また，視床痛の症例などでは，情動失禁や痛みに対する過剰反応を呈する症例が多くみられることから，中枢神経内での痛みの認知プロセスに対する効果についても検討する必要があるものと考える．抗不安薬あるいはマイナートランキライザーと呼ばれているベンゾジアゼピン系薬物はGABA$_A$受容体のGABA親和性を高めることが報告されており，GABAの作用を増強することによって効果を発現するものと考えられている．また，バルビツール酸系薬物も同様の効果が報告されている．カルバマゼピンは抗てんかん薬であるが，三叉神経痛や求心路遮断痛に効果を認める．また，痙攣の予防にも効果を認めるとの観点から，大脳皮質運動領刺激療法を施行中の症例には特に有用性が高い．

ケタミンの点滴を定期的に行い，経口薬を併用するケタミン点滴療法は，中枢性疼痛のみならず，幻肢痛や断端痛などの末梢性求心路遮断痛にも有効である．また，大脳皮質運動野刺激を施行している患者の除痛効果を増強することも可能であり[9-11]，今後の更なる発展が期待される

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特集 脳神経外科手術のモニタリング

運動野・錐体路におけるMEPモニタリングの実際

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Motor Evoked Potential (MEP) for the Intra-operative Monitoring of Motor Function

by

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Development of awake surgery has enabled us to monitor the fine movements of the extremities during neurosurgical operations. However, we can not employ awake surgery for the monitoring of motor function which includes the postoperative functional recovery, since it is well known that motor disturbance following injury of the supplementary motor cortex and premotor area recovers spontaneously within several weeks.

The warning criteria of the cortico-muscular motor evoked potential (MEP) differ among individual reports. This may reflect differences in the monitoring methods used, and we must set the warning criteria for application in individual institutes. The cortico-spinal MEP can be recorded stably and is suitable for the monitoring of motor function which includes the postoperative functional recovery. The subcortico-spinal MEP is especially useful for assessing the distance between the motor tract and operating fields.

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Key words : motor evoked potential, motor cortex, awake surgery, D-wave

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はじめに

脳脊髄の手術中に運動機能をモニターする方法として，覚醒下手術[4)5)8)]と運動誘発電位(motor evoked potential；MEP)[16)18)33)]が臨床応用されている．運動誘発電位という名称で一括されてはいるが，刺激装置には電気刺激装置と電磁刺激装置があり，刺激方法には直接に大脳皮質あるいは皮質下の脳組織を刺激する方法と経頭蓋的に刺激する方法がある．また，記録法には脊髄硬膜外から下行性の脊髄誘発電位を記録する方法と末梢の誘発筋電図を記録する方法がある．実際の運動誘発電位を用いた術中モニタリングには，それぞれの手術法を考慮して，刺激法と記録法の特性を考えた各種の組み合わせが臨床応用されてきた．しかしながら，電磁刺激[2)]は，手術器具の問題のみならず，安定した記録が得られにくいことから，術中の刺激には電気刺激が選択されている．脳手術中には，多くの症例で直接に大脳皮質を電気刺激することが可能である．一方，脊髄手術では，頭頂部に小穿

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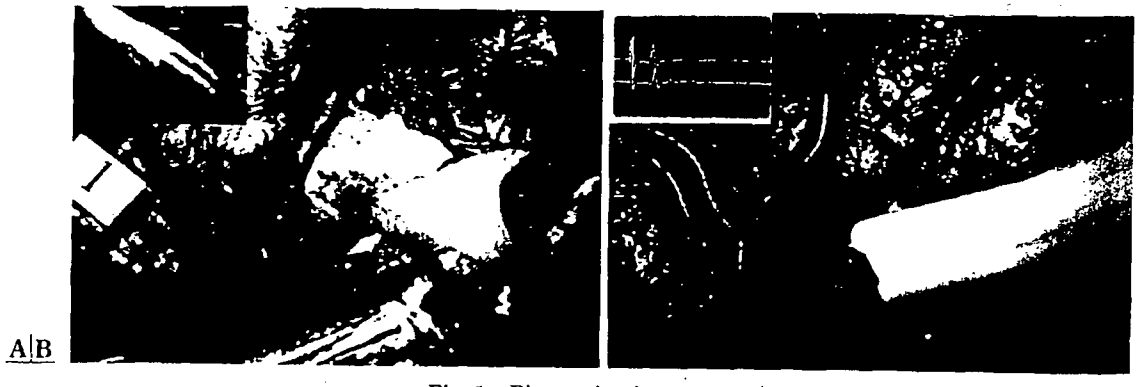

Fig. 1 Picture in picture system
Operator can watch voluntary movement of patient's extremities (A) and evoked potentials (B) in the field of microscope during the operation.

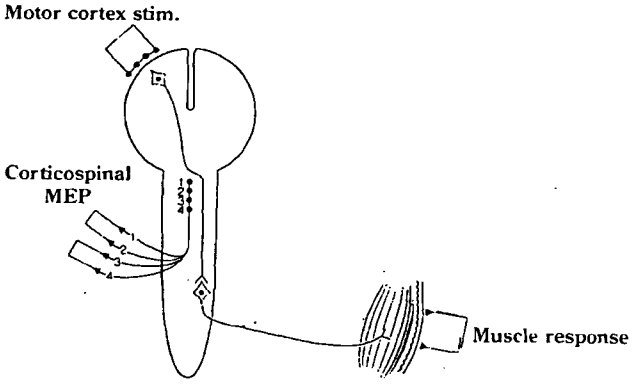

Fig. 2 Recording of cortico-muscular motor evoked potential (MEP) and cortico-spinal MEP
In cortico-muscular MEP monitoring, care needs to be exercised concerning the depth of anesthesia, use of muscle relaxant, and the excitability of spinal motoneurons. Corticospinal MEP monitoring requires that the recording electrode must be inserted into the cervical epidural space prior to the operation.

孔を設ける以外は直接に大脳皮質を電気刺激することが困難であり，経頭蓋刺激が用いられることが多い．

脊髄硬膜外やクモ膜下腔からの記録[9)15)16)26)27)]では，通常の全身麻酔が可能で筋弛緩や麻酔濃度に影響されないが，末梢の誘発筋電図を記録する方法[18)25)]では，麻酔薬，筋弛緩剤のみならず，笑気によっても誘発筋電図が抑制されるので，特別の注意が必要となる．

本稿では，覚醒下手術との比較を交えて，各種の運動誘発電位モニタリングの有用性と問題点について述べる．また，運動野近傍のグリオーマ例において，永続的な機能障害出現の有無を判定することが可能な方法について紹介したい．

各種の術中運動機能モニタリングの方法

1 覚醒下手術 (awake surgery)

静脈麻酔薬プロポフォール®の開発によって普及した方法で，開閉頭時には完全静脈麻酔として手術を行う．プロポフォール®の投与中止後10分程度で覚醒状態となるので，患者に四肢の自発運動を継続してもらい，この間に運動を確認しながら運動野近傍の腫瘍を摘出していく[4)5)8)]．われわれの施設では，picture in picture systemを用いることによって顕微鏡視野内に患者の四肢の状態を投影し，術者自身が患者の運動機能を迅速に把握できるようにしている (Fig. 1)．この顕微鏡視野内にはモニタリングを行う誘発電位などの波形を直接に投影することができるので，術者自身がモニタリング中の波形を確認することができる．

覚醒下手術では，実際に四肢の細かい運動を確認しつつ摘出を進めていくので，巧緻運動をモニタリングするには必須の手術法である．しかし，補足運動野や運動前野の障害で出現した運動障害が数週間で完全に回復してしまう事実[3)7)24)33)]を考慮すると，覚醒下手術では術後の機能回復を期待するまでの摘出は困難であり，安全圏の手術法といわざるをえない．